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# A randomized trial to manipulate the quality instead of quantity of dietary proteins to influence the markers of satiety☆,☆☆,★

Brooke E. Bayham, Frank L. Greenway, William D. Johnson, Nikhil V. Dhurandhar *

*Pennington Biomedical Research Center, Baton Rouge, LA*

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ABSTRACT

*Aims:* To test whether a breakfast including eggs (EB) containing high-quality protein decreases subsequent food intake and increases satiety-related hormones in overweight or obese adults more than a breakfast including cereal (CB) of lower protein quality, but matched for energy density and macronutrient composition.

*Methods:* Twenty healthy overweight or obese subjects were randomized to eat an EB or a CB daily under supervision for one week, followed by a crossover to the opposite breakfast week after a two-week washout period. On days 1 and 7 of each test week, a structured lunch was provided *ad libitum*. Food intake, hunger and satiety scores, and blood parameters were measured before and after breakfast. Outcomes were analyzed using mixed effects statistical models for repeated measures analysis of variance.

*Results:* Compared to the CB week, during the EB week, a) feeling of fullness was greater ($P < 0.05$) on day 1 but not on day 7; b) energy intake was not significantly lower on either day; c) right before lunch, acylated ghrelin was lower and PYY3-36 was higher on day 1 ($P < 0.01$ and $<0.002$, respectively) but not on day 7; d) PYY3-36, but not ghrelin, showed greater rise between breakfast and lunch on days 1($P < 0.001$) and 7 ($P < 0.01$).

*Conclusion:* Despite a highly similar energy density and macronutrient composition, the higher protein quality breakfast significantly influenced fullness, ghrelin and PYY3-36. Only the effect on PYY3-36 lasted throughout the week. A next step would be to test if the benefits are pronounced and lasting, if protein quality of all meals is increased.



## 1. Introduction

Weight loss is an effective measure in prevention and management of diabetes (Hamman, Wing, Edelstein, et al., 2006; Wing, 2010), and caloric restriction is the cornerstone of most weight loss approaches. However, long-term compliance with a reduced-energy diet is challenging (Holt, Brand-Miller, & Stitt, 2001). Therefore, additional supportive strategies such as nutritional approaches that enhance satiety are needed to increase compliance with weight loss diets. Foods differ in their ability to reduce hunger and increase satiety (Holt, Miller, Petocz, & Farmakalidis, 1995). Protein quantity is a factor positively correlated with satiety index score (SIS) of different test foods (Holt et al., 1995). This property of proteins has been exploited for weight loss. Clinical trials have shown that high protein diets result in greater short-term weight loss or fat loss (Larosa, Fry, Muesing, & Rosing, 1980; Layman, Boileau, Erickson, et al., 2003; Westman, Yancy, Edman, Tomlin, & Perkins, 2002), but the results are not maintained over time (Foster, Wyatt, Hill, et al., 2003; Nordmann, Nordmann, Briel, et al., 2006; Sacks, Bray, Carey, et al., 2009; Stern, Iqbal, Seshadri, et al., 2004). Thus, the role of increasing protein *quantity* to reduce energy intake has been questioned (Blatt, Roe, & Rolls, 2011). In addition, concerns about the potential adverse side effects of high protein diets have been expressed (Anderson, Konz, & Jenkins, 2000; Reddy, Wang, Sakhaee, Brinkley, & Pak, 2002). An alternative approach may be to focus on protein *quality*, instead of the *quantity*. The Protein Digestibility Corrected Amino Acid Score (PDCAAS) indicates the amino acid composition of the protein and thus reflects protein quality (Layman, 2004). Consuming greater amounts of high *quality* protein, particularly at breakfast, has been recommended for a favorable body composition change during weight loss (Layman, 2004). Also, breakfast foods with high SIS

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☆☆ Clinical trial registry: NCT01413217 (http://clinicaltrials.gov/ct2/show/NCT01413217).

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* Corresponding author at: Pennington Biomedical Research Center, Louisiana State University System, 6400 Perkins Road, Baton Rouge, LA 70808. Tel.: +1 225 763 2741; fax: +1 225 763 3030.

*E-mail address:* nikhil.dhurandhar@pbrc.edu (N.V. Dhurandhar).

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induce a greater feeling of fullness compared to those with lower SIS (Holt et al., 2001) and are also negatively correlated with energy intake at lunch (Holt et al., 2001). Therefore, we determined if the satiating effect of proteins could be harnessed by increasing the protein *quality* without increasing protein *quantity* in a test breakfast.

This study tested the hypothesis that an EB will induce greater satiety than a ready-to-eat CB that has lower protein quality but similar energy density (ED) and macronutrient composition. We opted to compare the two breakfasts for the following reasons: eggs are a common breakfast food with superior protein quality, have a 50% greater SIS than ready-to-eat (RTE) cereal (Holt et al., 1995) – another commonly consumed breakfast. Eggs and cereals have a PDCAAS of 100 and 42, respectively (Schaafsma, 2000). In addition, the two foods have a differing content of the branched chain amino acid (BCAA) leucine, an important contributor to protein quality (Layman & Walker, 2006; Norton, Wilson, Layman, Moulton, & Garlick, 2012). Since the EB had a greater PDCAAS and more than three times the amount of leucine than the CB, the EB was considered to be a relatively higher quality protein breakfast. We reasoned that if a test meal higher in protein quality enhances objective and subjective measures of satiety, then future weight loss trials may manipulate protein quality instead of quantity, which has not been tested in long term weight loss trials.

## 2. Subjects and methods

### 2.1. Ethics statement

This study was approved by the institutional review board at the Pennington Biomedical Research Center (PBRC; IRB#10010). Written informed consent was obtained from the subjects prior to the initiation of study procedures. The Study was conducted at PBRC, in an outpatient setting.

This trial was registered with Clinicaltrials.Gov (http://www.clinicaltrials.gov/) #NCT01413217 (http://www.clinicaltrials.gov/ct2/show/NCT01413217?term=eggs+Pennington&rank=2). Subjects were recruited starting July 2010. The last subject visit was on November 2, 2010. The trial ended as intended, when the study was completed.

### 2.2. Eligibility criteria

A telephone screening determined if the potential participants had a) BMI between 25 and 60 kg/m$^2$, b) age between 18 and 60 years, c) $\leq$5% body weight loss in the three months preceding the study. Those who qualified came to the clinic for a screening visit which included a history and physical examination to determine eligibility. Individuals with an unstable cardiac condition; major systemic illness; history of drug abuse or eating disorder; uncontrolled diabetes or hypothyroidism; familial hyperlipidemia; an allergy, sensitivity, or dislike of eggs, soy, or wheat; those attempting to lose weight; or those with an eating disorder were excluded from the study.

### 2.3. Subjects

Power calculations for determining the number of participants were based on our earlier study that used similar breakfasts (Vander Wal, Gupta, Khosla, & Dhurandhar, 2008). Of the 56 subjects screened for the study, 21 met the eligibility criteria and agreed to participate in the intervention trial. Subjects were randomly allocated (1:1 ratio) to one of two groups: (1) EB on test week 1 and CB on test week 2 or (0032) CB on test week 1 and EB on test week 2. The randomization sequence was compiled by the statistician (WDJ) using computer generated pseudo random numbers. The sequence was in alternating permuted blocks of sizes of 2 and 4. The statistician provided a list of the randomization schedule to the kitchen staff well trained in maintaining confidentiality of treatment allocation in randomized trials. Only the statistician and kitchen staff knew the group assignment for a specific participant until that participant was presented his first meal. Participants were instructed not to inform evaluation staff their breakfast type on a given day.

### 2.4. Procedures

In this randomized, crossover trial, each subject received two diets in a random order. Nine subjects were randomized to receive the EB, and 12 subjects were randomized to receive the CB during the first test week. On day one, subjects reported to the clinic following a 12-hour fast and were provided with breakfast at 8:00 AM, which they were required to consume completely. The two breakfasts were similar in weight (g), caloric content, and macronutrient composition (described below and in Table 1). After breakfast, subjects remained in the clinic and were provided a standardized lunch (described below) 180 minutes after they consumed breakfast. An intravenous line was placed in subject's forearm before breakfast to obtain blood samples until 120 minutes after consuming lunch. A questionnaire assessed satiety and hunger before and after breakfast and lunch (described below). To avoid an unintentional impact on food intake, the subjects were told the purported aim of the study was to determine the effect of breakfast on blood glucose and insulin, blood hormones and blood pressure. Subjects reported to the clinic for the next six days at 8:00 AM in a fasted state to eat the same breakfast consumed on day one. No blood samples were obtained and lunch was not provided on days 2–6. On day 7, the blood tests and questionnaires were repeated and food and water intake were measured following lunch. After the first test week, the subjects underwent a two-week washout period in which they consumed their usual pre-study breakfasts. Following the washout period, they returned for the second test week and the cycle was repeated with the opposite breakfast.

### 2.5. Breakfast and lunch

The EB contained two scrambled eggs, 120 mL skim milk, two slices of Holsum® thin white bread, 5 g of butter, and 18 g of Smuckers® strawberry jam. The CB contained 1.5 cups of Special K® RTE cereal, 200 ml Silk® original soymilk, one slice of Natural Grain "Wheat n' Fiber"® bread, 13 g of butter, and 10 g of sugar-free strawberry jam. The breakfasts were matched for ED and macronutrient composition but differed in PDCAAS (Schaafsma, 2000), leucine content, and glycemic load (Table 1). Glycemic load for foods was determined as previously described (Foster-Powell, Holt, & Brand-Miller, 2002). A standardized lunch consisting of lemon sage chicken, wild rice, mixed vegetables, a white dinner roll, canned pears, salted butter, 1% milk, and water was provided *ad libitum*. The amount of food and water consumed were covertly weighed before and after each subject was served.

**Table 1**
Energy density, macronutrient composition, and protein score of the breakfasts.

| | Egg breakfast | Cereal breakfast |
|---|---|---|
| Weight (g) | 291 | 293 |
| Energy (kcal) | 400 | 398 |
| Energy density (kcal/g) | 1.37 | 1.36 |
| Carbohydrate (%) | 42.9 | 44.8 |
| Fat (%) | 35.6 | 35.4 |
| Protein (%) | 19.8 | 19.8 |
| PDCAAS[1] | 100 | 42 |
| Leucine (g) | 1.77 | 0.48 |
| Glycemic load | 24 | 30.8 |
| Fiber (g) | 1.0 | 4.4 |

[1]Protein digestibility corrected amino acid score of egg proteins or wheat proteins.